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Date: February 6, 2007
Name: Margaret M. Gliaos
Signature: Margaret M. Gliaos
Gibbons, Del Deo, Dolan, Griffinger & Vecchione, P.C.

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

Applicant:	A.P. Kozokowski	Confirmation No.:	7176
Serial No.:	10/783,801		
Filed:	February 20, 2004	Customer No.:	26345
Title:	Synthesis of 4-α-Arylepicatechins		
Examiner:	Toafiq A. Solola		
TC/A.U.:	1626		

REQUEST FOR A CERTIFICATE OF CORRECTION

Honorable Commissioner for Patents
P.O. Box 1450
Alexandria, VA 22313-1450

Sir:

The error in the filing date of Serial No. 09/655,360 is a Patent Office printing error. The correct Domestic Priority date of 09/05/2000 is shown on the Corrected Filing Receipt attached as Exhibit 1.

The error in step (b) of Claim 2 is a Patent Office error. See the May 15, 2006 Response to Restriction Requirement where in step (b) of Claim 38 (Claim 2 of the '014 patent) "the C-4 position" is identified.

A copy of the Restriction Requirement is attached as Exhibit 2 (see Claim 38 on page 4).

Since these are Patent Office, errors no fee should be due.

CORRESPONDENCE AND FEES

In the event that any fees are required, authorization is hereby given to charge Deposit Account No. 03-3839. Please address all correspondence to Intellectual Property Docket Administrator, Gibbons, Del Deo, Dolan, Griffinger & Vecchione, One Riverfront Plaza, Newark, NJ 07102-5497.

Should there be any questions or other matters that may be resolved by a telephone call, the Examiner is invited to contact the undersigned attorney at the number below.

February 6, 2007

Respectfully submitted,

Gibbons, Del Deo, Dolan, Griffinger & Vecchione

By Margaret B Kelley

Margaret B. Kelley
Attorney for Applicant
Registration No. 29,181
Telephone No.: (212) 613-2000
Facsimile No.: (212) 554-9646

EXHIBIT 1

UNITED STATES PATENT AND TRADEMARK OFFICE

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APPL NO.	FILING OR 371 (c) DATE	ART UNIT	FIL FEE REC'D	ATTY.DOCKET NO	DRAWINGS	TOT CLMS	IND CLMS
10/783,801	02/20/2004	1626	770	5677-215		7	1

CONFIRMATION NO. 7176

Clifford Chance US LLP
200 Park Avenue
New York, NY 10166-0153

CORRECTED FILING RECEIPT

OC000000014878088

OC000000014878088

Date Mailed: 01/05/2005

Receipt is acknowledged of this regular Patent Application. It will be considered in its order and you will be notified as to the results of the examination. Be sure to provide the U.S. APPLICATION NUMBER, FILING DATE, NAME OF APPLICANT, and TITLE OF INVENTION when inquiring about this application. Fees transmitted by check or draft are subject to collection. Please verify the accuracy of the data presented on this receipt. **If an error is noted on this Filing Receipt, please write to the Office of Initial Patent Examination's Filing Receipt Corrections, facsimile number 703-746-9195. Please provide a copy of this Filing Receipt with the changes noted thereon. If you received a "Notice to File Missing Parts" for this application, please submit any corrections to this Filing Receipt with your reply to the Notice. When the USPTO processes the reply to the Notice, the USPTO will generate another Filing Receipt incorporating the requested corrections (if appropriate).**

Applicant(s)

Alan P. Kozikowski, Princeton, NJ;
Leo J. Romanczyk JR., Hackettstown, NJ;
Werner Tuckmantel, Washington, DC;

Assignment For Published Patent Application

Mars, Incorporated

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Domestic Priority data as claimed by applicant

This application is a DIV of 10/214,830 08/08/2002 PAT 6,720,432
which is a DIV of 09/655,360 09/05/2000 PAT 6,476,241

Foreign Applications

If Required, Foreign Filing License Granted: 10/08/2004

The country code and number of your priority application, to be used for filing abroad under the Paris Convention, is US10/783,801

Projected Publication Date: 01/20/2005

Non-Publication Request: No

Early Publication Request: No

Title

Synthesis of 4alpha-arylepicatechins

Preliminary Class

549

LICENSE FOR FOREIGN FILING UNDER
Title 35, United States Code, Section 184
Title 37, Code of Federal Regulations, 5.11 & 5.15

GRANTED

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EXHIBIT 2

CERTIFICATE OF MAILING/FAX TRANSMISSION
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Name: Margaret M. Gliaos
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Gibbons, Del Deo, Dolan, Griffinger & Vecchione, P.C.

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

Applicant: A.P. Kozokowski Confirmation No.: 7176

Serial No.: 10/783,901

Filed: February 20, 2004 Customer No.: 26345

Title: Synthesis of 4-α-Arylepicatechins

Examiner: Toafiq A. Solola

TC/A.U.: 1626

RESPONSE TO RESTRICTION REQUIREMENT

Honorable Commissioner for Patents
P.O. Box 1450
Alexandria, VA 22313-1450

Sir:

This is submitted in response to the Restriction Requirement mailed April 14, 2006. A response is due May 16, 2006.

Amendment to the claims begins on page 2.

The Restriction Requirement begins on page 10.

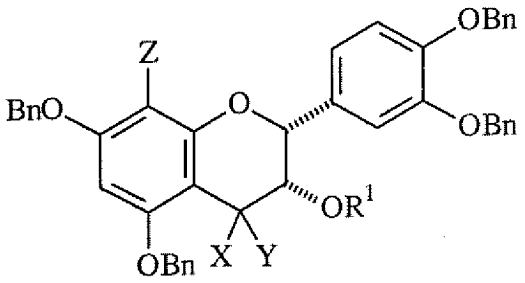
Remarks begin on page 11.

LISTING OF THE CLAIMS:

This listing of claims replaces all prior versions and listings of claims in this application.

Claims 1-21 (canceled)

Claim 22 (previously presented) A compound having the formula:



wherein R^1 is a silyl protecting group or a benzyl protecting group, wherein X and Y are independently hydrogen or hydroxy, and wherein Z is a hydrogen.

Claims 23-24 (canceled)

Claim 25 (previously presented) The compound of Claim 22, wherein R^1 is the silyl protecting group.

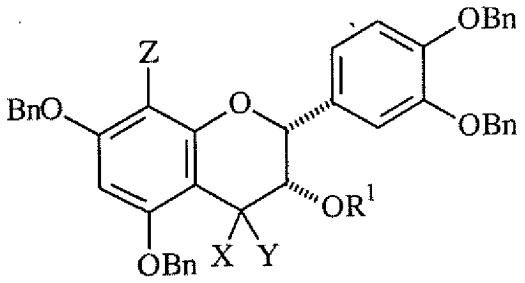
Claim 26 (previously presented) The compound of Claim 25, wherein the silyl group is a *tert*-butyldimethylsilyl group.

Claim 27 (previously presented) The compound of Claim 22, wherein R^1 is the benzyl protecting group.

Claims 28-30 (canceled)

Claim 31 (previously presented) The compound of Claim 22, which is 3, 5, 7, 3', 4'-penta-O-benzyl-4-hydroxyepicatechin or 5, 7, 3', 4'-tetra-O-benzyl-3-O-(*tert*-butyldimethylsilyl)-4-hydroxyepicatechin.

Claim 32 (previously presented) A compound having the formula:



wherein R^1 is a silyl protecting group or a benzyl protecting group, wherein X and Y together are oxygen, and wherein Z is hydrogen.

Claim 33 (currently amended) The compound of Claim 32, wherein [[R1]] $\underline{R^1}$ is the silyl protecting group.

Claim 34 (previously presented) The compound of Claim 33, wherein the silyl group is a *tert*-butyldimethylsilyl group.

Claim 35 (currently amended) The compound of Claim 32, wherein [[R1]] $\underline{R^1}$ is the benzyl protecting group.

Claim 36 (currently amended) The compound of Claim 32, which is ~~(2R,3S)-3,5,7,3',4'-pentakis-(benzyloxy)-flavan-4-one~~ (2R,3S)-3,5,7,3',4'-pentakis-(benzyloxy)flavan-4-one or ~~(2R,3S)-5,7,3',4'-tetra-O-benzyl-3-O-[(*tert*-butyldimethylsilyl)-oxy]-flavan-4-one~~ (2R,3S)-5,7,3',4'-tetra-O-benzyl-3-O-[(*tert*-butyldimethylsilyl)oxy]flavan-4-one.

Claim 37 (previously presented) A process for preparing epicatechin-(4α,8)-catechin dimer, which process comprise the steps of:

(a) protecting the 3-hydroxyl group of 5,7,3',4'-tetra-O-benzyl-epicatechin with a benzyl protecting group to form 3,5,7,3',4'-penta-O-benzyl-epicatechin;

(b) oxidizing the C-4 position of the epicatechin of step (a) to form 3,5,7,3',4'-penta-O-benzyl-4-hydroxy-epicatechin;

(c) oxidizing the C-4 hydroxyl group of the epicatechin of step (b) to form (2R,3S)-3,5,7,3',4'-penta-O-benzyl-4-ketone-epicatechin;

(d) adding *tert*-butyl lithium to 3,5,7,3',4'-penta-O-benzyl-8-bromo-catechin to form a catechin-lithium reagent;

(e) adding the epicatechin from step (c) to the catechin-lithium reagent from step (d) to form 3,5,7,3',4'-penta-O-benzyl-4-hydroxy-epicatechin-(4α,8)-(3,5,7,3',4'-penta-O-benzyl)-catechin dimer;

(f) reducing the C-4 hydroxyl group of the dimer from step (e) to form 3,5,7,3',4'-penta-O-benzyl-epicatechin-(4α,8)-(3,5,7,3',4'-penta-O-benzyl)-catechin dimer; and

(g) replacing the benzyl groups of the dimer of step (f) with hydrogen to form the epicatechin-(4α,8)-catechin dimer

Claim 38 (previously presented) A process for preparing 5,7,3',4'-tetra-O-benzyl-3-O-(*tert*-butyldimethylsilyl)-epicatechin-4α,8-[5,7,3',4'-tetra-O-benzyl-3-O-(*tert*-butyldimethylsilyl]-catechin dimer comprises the steps of:

(a) protecting the C-3 hydroxyl group of 5,7,3',4'-tetra-O-benzylepicatechin with a *tert*-butyldimethylsilyl group to form 5,7,3',4'-tetra-O-benzyl-C-3-O-(*tert*-butyldimethylsilyl)-epicatechin;

(b) oxidizing the C-4 position of the epicatechin from step (a) to form 5,7,3',4'-tetra-O-benzyl-3-O-(*tert*-butyldimethylsilyl)-4-hydroxy-epicatechin;

(c) oxidizing the C-4 hydroxyl group of the epicatechin from step (b) to form (2R,3S)-5,7,3',4'-tetra-O-benzyl-3-O-(*tert*-butyldimethylsilyl)-4-ketone-epicatechin;

(d) adding *tert*-butyllithium to 5,7,3',4'-tetra-O-benzyl-8-bromo-3-O-(*tert*-butyldimethylsilyl)-catechin to form a catechin-lithium reagent;

(e) adding the epicatechin from step (c) to the catechin-lithium reagent from step (d) to form 5,7,3',4'-tetra-O-benzyl-3-O-(*tert*-butyldimethylsilyl)-4-hydroxy-epicatechin-4α,8-[5,7,3',4'-tetra-O-benzyl-3-O-(*tert*-butyldimethylsilyl)-catechin dimer;

(f) reducing the C-4 hydroxyl group of the dimer from step (e) to form the 5,7,3',4'-tetra-O-benzyl-3-O-(*tert*-butyldimethylsilyl)-epicatechin-4α,8-[5,7,3',4'-tetra-O-benzyl-3-O-(*tert*-butyldimethylsilyl)]-catechin dimer.

Claim 39 (previously presented) A process for preparing an epicatechin-(4α,8)-(3-O-acyl)-catechin dimer comprises the steps of:

(a) protecting the C-3 hydroxyl group of 5,7,3',4'-tetra-O-benzyl-epicatechin with a *tert*-butyldimethylsilyl group to form 5,7,3',4'-tetra-O-benzyl-C-3-O-(*tert*-butyldimethylsilyl)-epicatechin;

(b) oxidizing the C-4 position of the epicatechin from step (a) to form 5,7,3',4'-tetra-O-benzyl-3-O-(*tert*-butyldimethylsilyl)-4-hydroxy-epicatechin;

(c) oxidizing the C-4 hydroxyl group of the epicatechin from step (b) to form (2R,3S)-5,7,3',4'-tetra-O-benzyl-3-O-*tert*-butyldimethylsilyl-4-ketone-epicatechin;

(d) adding *tert*-butyl lithium to 5,7,3',4'-tetra-O-benzyl-8-bromo-3-O-(*tert*-butyldimethylsilyl) catechin to form a catechin-lithium reagent;

(e) adding the epicatechin from step (c) to the catechin-lithium reagent from step (d) to form 5,7,3',4'-tetra-O-benzyl-3-O-(*tert*-butyldimethylsilyl)-4-hydroxy-epicatechin-(4α,8)-[5,7,3',4'-tetra-O-benzyl-3-O-(*tert*-butyldimethylsilyl)]-catechin dimer;

(f) reducing the C-4 hydroxyl group of the dimer from step (e) to form 5,7,3',4'-tetra-O-benzyl-3-O-(*tert*-butyldimethylsilyl)-epicatechin-(4α,8)-[5,7,3',4'-tetra-O-benzyl-3-O-(*tert*-butyldimethylsilyl)]-catechin dimer;

(g) replacing the *tert*-butyldimethylsilyl protecting groups of the dimer of step (f) with hydrogen to form 5,7,3',4'-tetra-O-benzyl-epicatechin-(4α,8)-(tetra-O-benzyl-catechin)-dimer;

(h) acylating the 3-OH position of the dimer of step (g) with an activated acid or an acid chloride to form a 5,7,3',4'-tetra-O-benzyl-epicatechin-(4α,8)-[5,7,3',4'-tetra-O-benzyl-(3-O-acyl) catechin]-dimer; and

(i) replacing the benzyl protecting groups of the dimer from step (h) with hydrogen to form the epicatechin –(4α,8)-(3-O-acyl)-catechin dimer.

Claim 40 (previously presented) The process of Claim 37, wherein the protecting step (a) is carried out with benzyl bromide in the presence of sodium hydride; wherein the oxidizing step (b) is carried out with 2,3-dichloro-5,6-dicyano-p-benzoquinone and 4-(dimethylamino) pyridine; wherein the oxidizing step (c) is carried out with tetrapropylammonium perruthenate and N-methylmorpholine-N-oxide; wherein the reducing step (f) is carried out with tri-n-butyltin hydride followed by trifluoroacetic acid; and wherein the benzyl replacement step (g) is carried out by hydrogenation in the presence of palladium hydroxide on carbon.

Claim 41 (previously presented) The process of Claim 38, wherein the protecting step (a) is carried out with *tert*-butyldimethylsilyl chloride; wherein the oxidizing step (b) is carried out with 2,3-dichloro-5,6-dicyano-*p*-benzoquinone and 4-(dimethylamino) pyridine; wherein the oxidizing step (c) is carried out with N-methylmorpholine-N-oxide and tetrapropylammonium perruthenate; and wherein the reducing step (f) is carried out with tri-*n*-butyltin hydride and trifluoroacetic acid.

Claim 42 (previously presented) The process of Claim 39, wherein the protecting step (a) is carried out with *tert*-butyldimethylsilyl chloride; wherein the oxidizing step (b) is carried out with 2,3-dichloro-5,6-dicyano-*p*-benzoquinone and 4-(dimethylamino) pyridine; wherein the oxidizing step (c) is carried out with N-methylmorpholine-N-oxide and terapropylammonium perruthenate; wherein the reducing step (f) is carried out with tri-n-butyltin hydride and trifluoroacetic acid; wherein the *tert*-butyldimethylsilyl replacement step (g) is carried out with hydrofluoric acid; and wherein the benzyl replacement step (i) is carried out by hydrogenation in the presence of palladium hydroxide on carbon.

Claim 43 (previously presented) The process of Claim 39, wherein the acid is selected from group consisting of caffeic, coumaric, ferulic, and sinapic acid.

Claim 44 (previously presented) The process of Claim 39, wherein the acid is a hydroxy-protected acid selected from the group consisting of cinnamic acid, gallic acid, and hydroxybenzoic acid.

Claim 45 (previously presented) The process of Claim 39, wherein the acid is tri-O-benzylgallic acid and the epicatechin-(4α, 8)-(3-O-acyl)-catechin dimer is epicatechin-4α,8-(3-O-galloyl)-catechin dimer.

Claim 46 (currently amended) A protected dimer selected from the group consisting of 5,7,3',4'-tetra-O-benzyl-3-O-(*tert*-butyldimethylsilyl)-epicatechin-(4α,8)-[5,7,3',4'-tetra-O-benzyl-3-O(*tert*-butyldimethylsilyl)]-catechin; 3,5,7,3',4'-penta-O-benzyl-epicatechin-(4α,8)-(3,5,7,3',4'-penta-O-benzyl-catechin); and 5,7,3',4'-tetra-O-benzyl-epicatechin-(4α,8)-(5,7,3',4'-tetra-O-benzyl-catechin).

Claim 47 (previously presented) A protected epicatechin-(4α,8)-catechin dimer having a 4-hydroxy group selected from the group consisting of 5,7,3',4'-tetra-O-benzyl-3-O-

(*tert*-butyldimethylsilyl)-4-hydroxy-epicatechin-(4α,8)-[5,7,3',4'-tetra-O-benzyl-3-O-(*tert*-butyldimethylsilyl)catechin] and 3,5,7,3',4'-penta-O-benzyl-4-hydroxy-epicatechin-(4α,8)-(penta-O-benzyl-catechin).

Claim 48 (previously presented) A derivatized 5,7,3',4'-tetra-O-benzyl-epicatechin-(4α,8)-(5,7,3',4'-tetra-O-benzyl-catechin) dimer having at least one 3-O-acyl group.

Claim 49 (previously presented) The dimer of Claim 48, wherein the 3-O-acyl group is introduced using an acid selected from the group consisting of caffeic acid, coumaric, ferulic acid, and sinapic acid as a derivatizing agent.

Claim 50 (previously presented) The dimer of Claim 48 which is epicatechin-(4α,8)-[(3-O-acyl)-catechin].

Claim 51 (previously presented) The dimer of Claim 48, wherein the 3-O-acyl group is introduced using a hydroxy-protected acid selected from the group consisting of cinnamic acid, gallic acid, and hydroxy-benzoic acid as a derivatizing agent.

Claim 52 (previously presented) The dimer of Claim 51, wherein the 3-O-acyl group is a 3-O-(3,4,5-tri-O-benzylgalloyl) group.

Claim 53 (previously presented) The dimer of Claim 52 which is epicatechin-(4α,8)-[(3-O-galloyl)-catechin].

Claim 54 (previously presented) An epicatechin-(4α,8)-catechin dimer.

RESTRICTION REQUIREMENT

Restriction has been required as follows:

Group I - Claims 22, 25-27, 31-36 directed to tetra-O-benzyl-protected monomers having a benzyl or a silyl protecting group at C-3, e.g., 3,5,7,3',4'-penta-O-benzyl-3-O-benzyl-4-hydroxy-epicatechin or 5,7,3',4'-tetra-O-benzyl-3-O-*tert*-butyl-dimethylsilyl-4-hydroxy-epicatechin, (2R,3S)-5,7,3',4'-tetra-O-benzyl-3-O-[(*tert*-butyldimethylsilyl)oxy]-flavan-4-one, or (2R,3S)-3,5,7,3',4'-pentakis(benzyloxy)-flavan-4-one;

Group II - Claims 37 and 40 directed to a process for making an epicatechin dimer, specifically an EC-(4α,8)-C dimer;

Group III - Claims 38 and 41 directed to a process for making the compounds of Group I;

Group IV - Claims 39 and 42-45 directed to a process for making an EC-3-O-acyl dimer, e.g., EC-(4α,8)-3-O-galloyl-C dimer;

Group V - Claims 46-47 directed to specific protected dimers; e.g., 5,7,3',4'-tetra-O-benzyl-3-O-*(tert*-butyldimerthylsilyl)-EC-(4α,8)-5,7,3',4'-tetra-O-benzyl-3-O-*(tert*-butyldimerthylsilyl)-C or 3,5,7,3',4'-penta-O-benzyl-(4α,8)-3,5,7,3',4'-penta-O-benzyl-C, or 5,7,3',4'-tetra-O-benzyl-EC-(4α,8)-tetra-O-benzyl-C;

Group VI - Claims 48-53 directed to a tetra-O-benzyl-protected-(4α,8)-dimer having at least one 3-O-acyl group, e.g., EC-(4α,8)-[3-O-galloyl)-C]; and

Group VII - Claim 54 directed to an EC-(4α,8)-C dimer.

REMARKS

Applicants elect with traverse the claims of Group II, i.e., Claims 37 and 40 directed to a process for making an epicatechin-(4α,8)-catechin dimer. It is respectfully requested that the claim of Group VII, which is directed to the same dimer, i.e., an epicatechin-4α,8-catechin dimer, be examined at the same time. It would appear that a separate search would not be required or, if required, would not be unduly time consuming.

It is respectfully pointed out that the claims of Group III, i.e., Claims 38 and 44, are not directed to a process for making the compounds of Group I. The compounds of Group I are protected monomers, whereas the compounds made by the process of Claims 38 and 41 are protected dimers.

It is also respectfully pointed out that most of the claims do not cover a large number of compounds. Claims 37, 40, and 54 are all directed to one specific dimer, i.e., an EC-(4α,8)-C dimer.

CORRESPONDENCE AND FEES

In the event that any fees are required, authorization is hereby given to charge Deposit Account No. 03-3839. Please address all correspondence to Intellectual Property Docket Administrator, Gibbons, Del Deo, Dolan, Griffinger & Vecchione, One Riverfront Plaza, Newark, NJ 07102-5497.

Should there be any questions or other matters that may be resolved by a telephone call, the Examiner is invited to contact the undersigned attorney at the number below.

May 15, 2006

Respectfully submitted,

Gibbons, Del Deo, Dolan, Griffinger & Vecchione

By Margaret B. Kelley

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Total Number of Pages in This Submission: 12

Application Number	10/783,901
Filing Date	2/20/04
First Named Inventor	A.P. Kozlowski
Art Unit	1629
Examiner Name	Tariq A. Bokta
Attorney Docket Number	106942-53020

ENCLOSURES *(Check all that apply)*

- ☐ Fee Transmittal Form
- ☐ Fee Attached
- ☐ Amendment/Reply
- ☐ After Final
- ☐ Affidavits/declaration(s)
- ☐ Extension of Time Request
- ☐ Express Abandonment Request
- ☐ Information Disclosure Statement
- ☐ Certified Copy of Priority Document(s)
- ☐ Reply to Missing Parts/ Incomplete Application
- ☐ Reply to Missing Parts under 37 CFR 1.52 or 1.53
- ☐ Drawing(s)
- ☐ Licensing-related Papers
- ☐ Petition
- ☐ Petition to Convert to a Provisional Application
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- ☐ CD, Number of CD(s) _____
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- ☐ After Allowance Communication to TC
- ☐ Appeal Communication to Board of Appeals and Interferences
- ☐ Appeal Communication to TC (Appeal Notice, Brief, Reply Brief)
- ☐ Proprietary Information
- ☐ Status Letter
- ☑ Other Enclosure(s) (please identify below): Response to Restriction Requirement

Remarks

SIGNATURE OF APPLICANT, ATTORNEY, OR AGENT

Firm Name	Gibbons, Del Deo, Dolan, Griffinger & Vecchione, P.C.		
Signature	Margaret B. Kelley		
Printed name	Margaret B. Kelley	Reg. No.	39,181
Date	May 15, 2006		

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UNITED STATES PATENT AND TRADEMARK OFFICE
CERTIFICATE OF CORRECTION

PATENT NO : 7,126,014 B2

DATED : 10/24/2006

INVENTOR(S) : Kozikowski, et al.

It is certified that error appears in the above-identified patent and that said Letters Patent is hereby corrected as shown below:

at (62) delete "Sep. 5, 2001" and insert

-- filed on Sep. 5, 2000 --

in Claim 2, at column 21, line 20, rewrite "the C-3 position" as

-- the C-4 position --

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